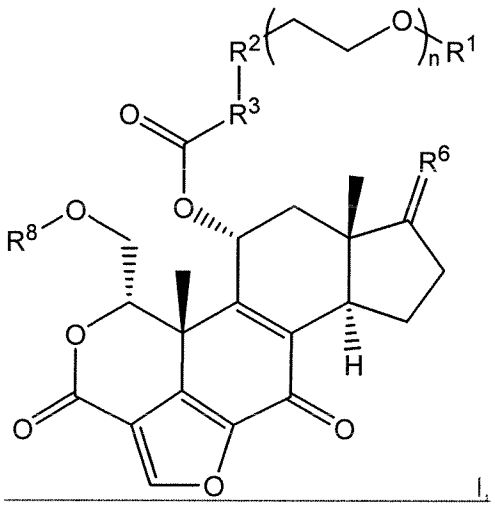
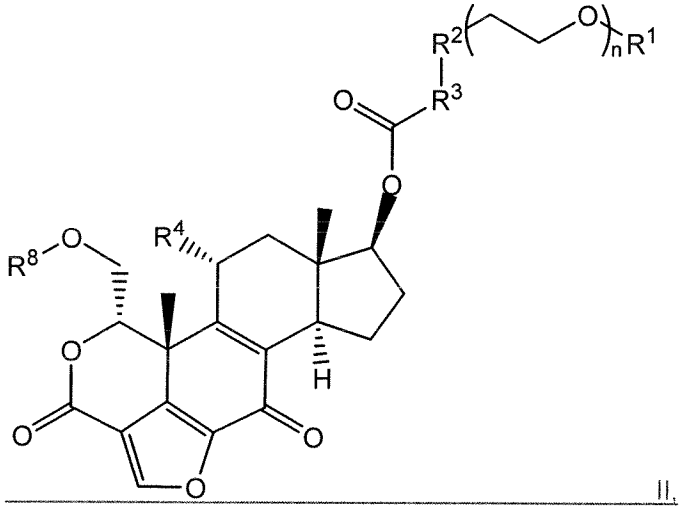
LISTING OF CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in this application.

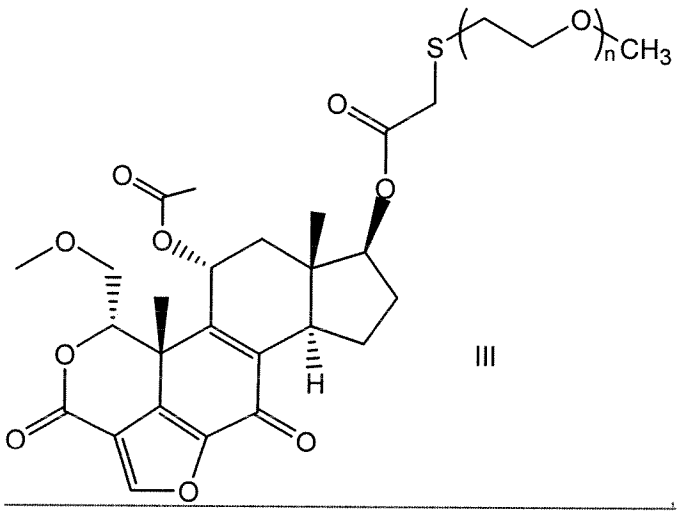
1. (Currently Amended) A water-soluble drug-polymer conjugate selected from a conjugate of formula I, II, III, IV and V:



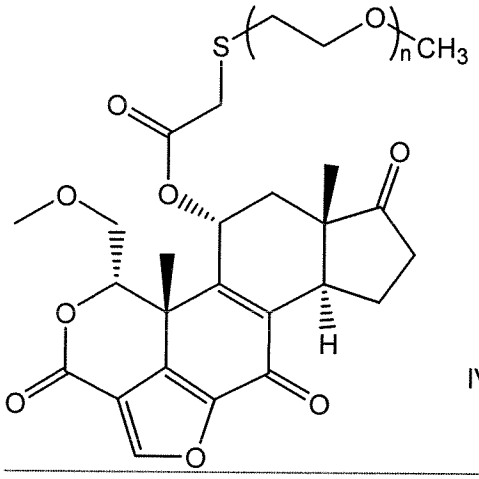
I,



II,

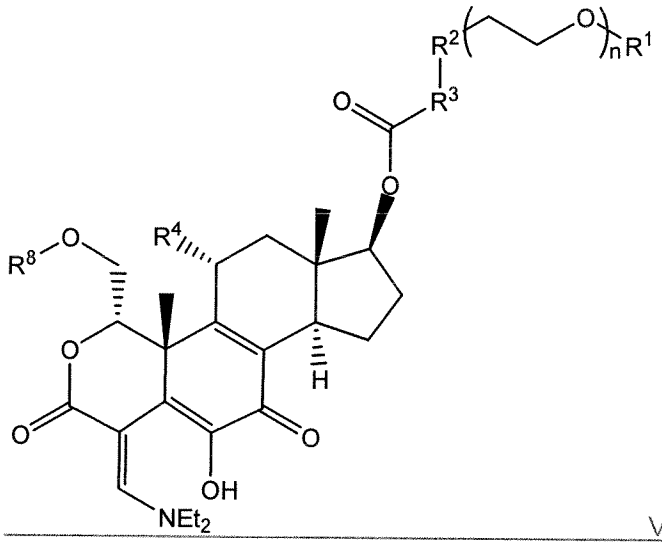


III



IV

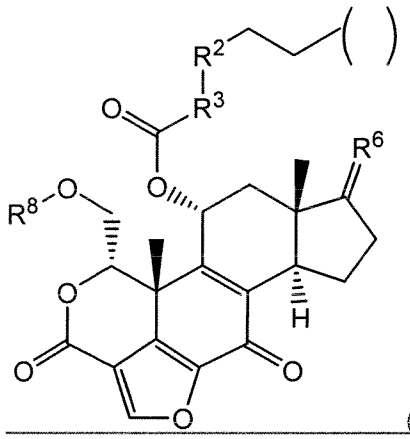
, and



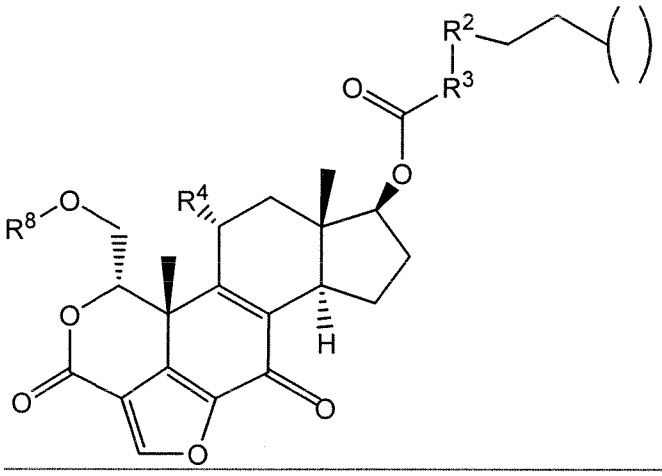
V,

wherein

R^1 is alkyl, a drug-polymer conjugate of formula (A) or a drug-polymer conjugate of formula (B):



(A)



(B);

R^2 is -O-, -NH-, or -S-;

R^3 is alkyl, a cycloalkyl, or aryl;

R^4 is H, =O, -O-COC_4H_9, or OR^7;

R^6 is =O or OR^7;

R^7 is H, COR^9 or alkyl;

R^8 is alkyl or H;

R^9 is alkyl, H, aryl, or $-CH_2Ar$; and

n is 1-1000 ~~having the general formula P--X-D: wherein, P is a water-soluble polymer; D is a wortmannin derivative; and X is a covalent linkage between a water-soluble polymer and the wortmannin derivative~~.

2. (Original) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 1 and a pharmaceutically acceptable carrier.

3. (Original) A method for treating or inhibiting a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 1.

4. (Original) A method of claim 3 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.

5. (Original) A method of claim 3 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.

6. (Original) A method of claim 3 wherein treating or inhibiting comprises inhibition of PI3 kinase.

7. (Original) A method of claim 3 wherein treating or inhibiting comprises inhibition of TOR kinase.

8. (Original) A method of claim 3 wherein the pathological condition is non-small cell lung cancer.

9. (Withdrawn) A method of claim 3 wherein the pathological condition is brain cancer, iscaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.

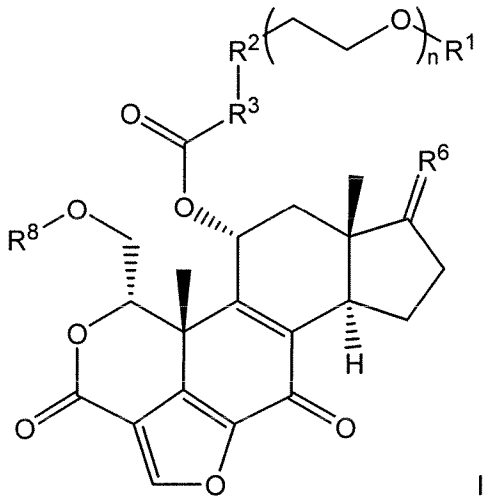
10. (Withdrawn) A method of claim 3 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.

11. (Withdrawn) A method of claim 10 wherein the agent is interferon-α.

12. (Withdrawn) A method of claim 10 wherein the agent is pegylated rapamycin.

13. (Withdrawn) A method of claim 10 wherein the agent is a cytotoxic.

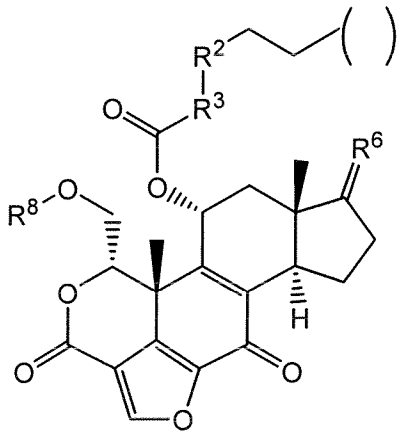
14. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula I



I

wherein:

R^1 is alkyl, or a drug-polymer conjugate of formula (A)



(A);

R^2 is -O-, -NH-, or -S-;

R^3 is alkyl, a cycloalkyl, or aryl;

R^6 is =O or OR^7;

R^7 is H, COR^9 or alkyl;

R^8 is alkyl or H;

R^9 is alkyl, H, aryl, or $-CH_2Ar$; and

n is 1-1000.

15. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein n is 250 – 400.

16. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein n is 50 – 150.

17. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein the molecular weight of polymer is from about 400 to about 80,000.

18. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein the molecular weight of polymer from about 1000 to about 8000.

19. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein the molecular weight of polymer is from about 4000 to about 6000.

20. (Withdrawn) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 14 and a pharmaceutically acceptable carrier.

21. (Withdrawn) A method for treating or inhibiting a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 14.

22. (Withdrawn) A method of claim 21 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.

23. (Withdrawn) A method of claim 21 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.

24. (Withdrawn) A method of claim 21 wherein treating or inhibiting comprises inhibition of PI3 kinase.

25. (Withdrawn) A method of claim 21 wherein treating or inhibiting comprises inhibition of TOR kinase.

26. (Withdrawn) A method of claim 21 wherein the pathological condition is non-small cell lung cancer.

27. (Withdrawn) A method of claim 21 wherein the pathological condition is brain cancer, iscaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.

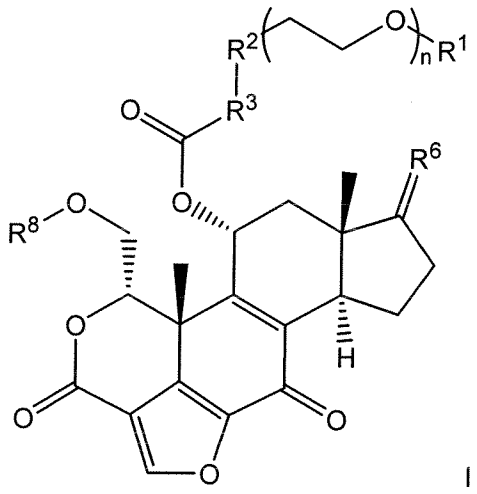
28. (Withdrawn) A method of claim 21 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.

29. (Withdrawn) A method of claim 28 wherein the agent is interferon-α.

30. (Withdrawn) A method of claim 28 wherein the agent is pegylated rapamycin.

31. (Withdrawn) A method of claim 28 wherein the agent is a cytotoxic.

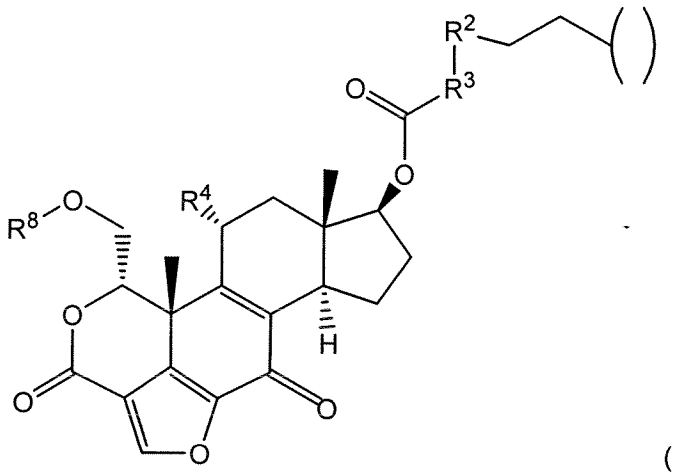
32. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula I:



I

wherein:

R^1 is alkyl, or a drug-polymer conjugate of formula (B)



(B);

R^2 is -O-, -NH-, or -S-;

R^3 is alkyl, a cycloalkyl, or aryl;

R^4 is H, =O, -O-COC_4H_9, or OR^7;

R^7 is H, COR^9 or alkyl;

R^8 is alkyl or H;

R^9 is alkyl, H, aryl, or $-CH_2Ar$; and

n is 1-1000.

33. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein n is 250 – 400.

34. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein n is 50 – 150.

35. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein the molecular weight of polymer is from about 400 to about 80,000.

36. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein the molecular weight of polymer is from about 1000 to about 8000.

37. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein the molecular weight of polymer is from about 4000 to about 6000.

38. (Withdrawn) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 32 and a pharmaceutically acceptable carrier.

39. (Withdrawn) A method for treating or inhibiting a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 32.

40. (Withdrawn) A method of claim 39 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.

41. (Withdrawn) A method of claim 39 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.

42. (Withdrawn) A method of claim 39 wherein treating or inhibiting comprises inhibition of PI3 kinase.

43. (Withdrawn) A method of claim 39 wherein treating or inhibiting comprises inhibition of TOR kinase.

44. (Withdrawn) A method of claim 39 wherein the pathological condition is non-small cell lung cancer.

45. (Withdrawn) A method of claim 39 wherein the pathological condition is brain cancer, iscaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.

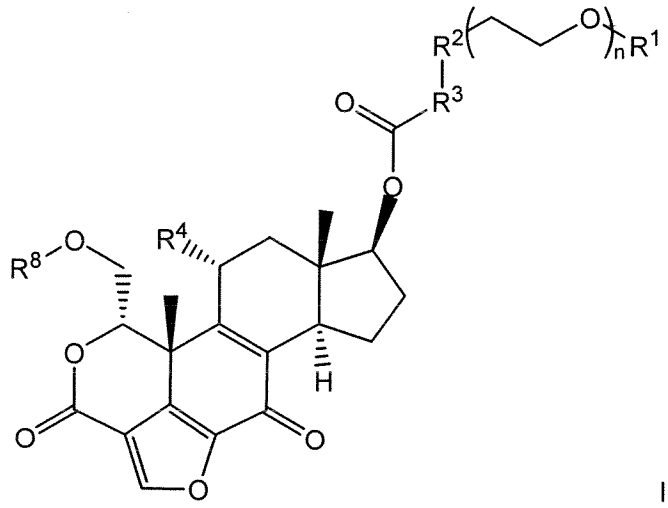
46. (Withdrawn) A method of claim 39 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.

47. (Withdrawn) A method of claim 46 wherein the agent is interferon-α.

48. (Withdrawn) A method of claim 46 wherein the agent is pegylated rapamycin.

49. (Withdrawn) A method of claim 46 wherein the agent is a cytotoxic.

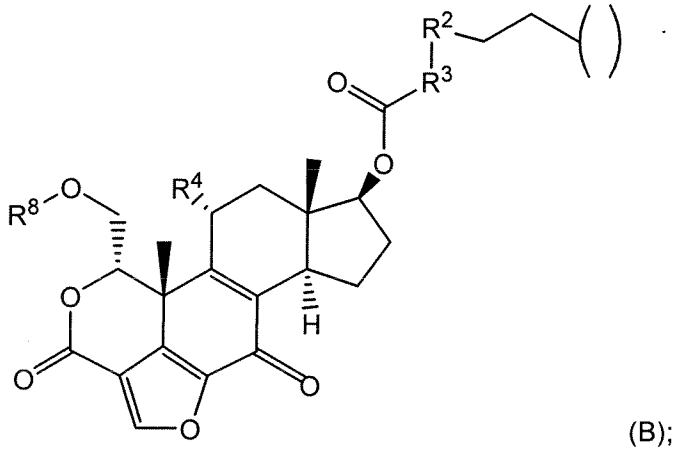
50. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula II



II

wherein:

R^1 is alkyl, or a drug-polymer conjugate of formula (B)



(B);

R^2 is -O-, -NH-, or -S-;

R^3 is alkyl, a cycloalkyl, or aryl;

R^4 is H, =O, -O-COC_4H_9, or OR^7;

R^7 is H, COR^9 or alkyl;

R^8 is alkyl or H;

R^9 is alkyl, H, aryl, or $-CH_2Ar$; and

n is 1-1000.

51. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein n is 250 – 400.

52. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein n is 50 – 150.

53. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein the molecular weight of polymer is from about 400 to about 80,000.

54. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein the molecular weight of polymer is from about 1000 to about 8000.

55. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein the molecular weight of polymer is from about 4000 to about 6000.

56. (Withdrawn) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 50 and a pharmaceutically acceptable carrier.

57. (Withdrawn) A method for treating or inhibiting a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 50.

58. (Withdrawn) A method of claim 57 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.

59. (Withdrawn) A method of claim 57 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.

60. (Withdrawn) A method of claim 57 wherein treating or inhibiting comprises inhibition of PI3 kinase.

61. (Withdrawn) A method of claim 57 wherein treating or inhibiting comprises inhibition of TOR kinase.

62. (Withdrawn) A method of claim 57 wherein the pathological condition is non-small cell lung cancer.

63. (Withdrawn) A method of claim 57 wherein the pathological condition is brain cancer, iscaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.

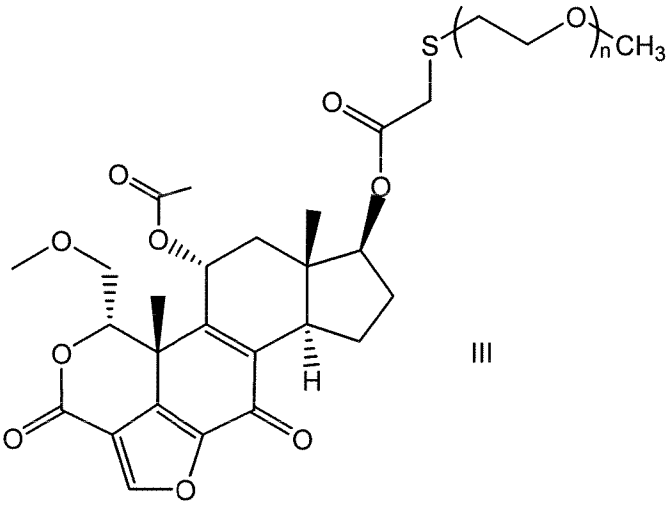
64. (Withdrawn) A method of claim 57 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.

65. (Withdrawn) A method of claim 64 wherein the agent is interferon-α.

66. (Withdrawn) A method of claim 64 wherein the agent is pegylated rapamycin.

67. (Withdrawn) A method of claim 64 wherein the agent is a cytotoxic.

68. (Original) A water-soluble drug-polymer conjugate having the structure of formula III:



III

n is 1-1000.

69. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein n is 250-400.

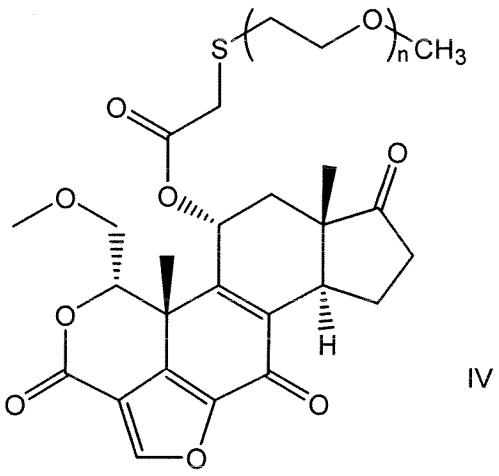
70. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein n is 50-150.

71. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein the molecular weight of polymer is from about 400 to about 80,000.

72. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein the molecular weight of polymer is from about 1000 to about 8000.

73. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein the molecular weight of polymer is from about 4000 to about 6000.

74. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula IV:



IV

wherein n = 1-1000.

75. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein n is 250 – 400.

76. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein n is 50 – 150.

77. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein the molecular weight of polymer is from about 400 to about 80,000.

78. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein the molecular weight of polymer is from about 1000 to about 8000.

79. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein the molecular weight of polymer is from about 4000 to about 6000.

80. (Withdrawn) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 74 and a pharmaceutically acceptable carrier.

81. (Withdrawn) A method for treating or inhibiting a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 74.

82. (Withdrawn) A method of claim 81 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.

83. (Withdrawn) A method of claim 81 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.

84. (Withdrawn) A method of claim 81 wherein treating or inhibiting comprises inhibition of PI3 kinase.

85. (Withdrawn) A method of claim 81 wherein treating or inhibiting comprises inhibition of TOR kinase.

86. (Withdrawn) A method of claim 81 wherein the pathological condition is non-small cell lung cancer.

87. (Withdrawn) A method of claim 81 wherein the pathological condition is brain cancer, iscaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.

88. (Withdrawn) A method of claim 81 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.

89. (Withdrawn) A method of claim 88 wherein the agent is interferon-α.

90. (Withdrawn) A method of claim 88 wherein the agent is pegylated rapamycin.

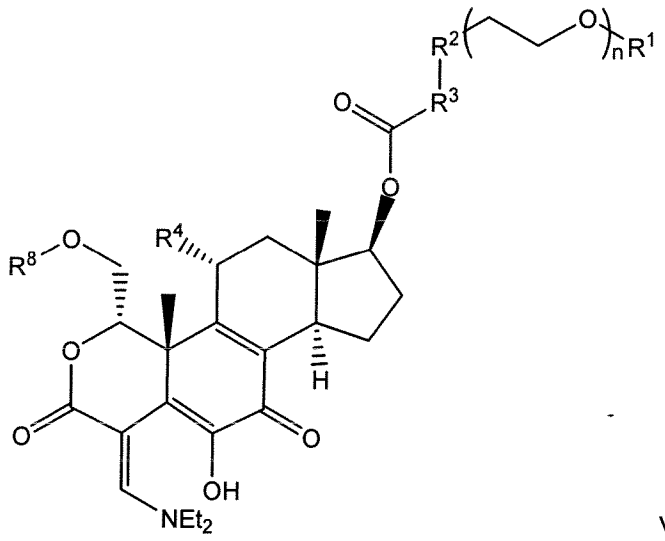
91. (Withdrawn) A method of claim 88 wherein the agent is a cytotoxic.

92. (Withdrawn) A process for the preparation of a water-soluble drug-polymer conjugate of claim 68 comprising:

a. adding a solvent to 17-dihydro-17-(1-iodoacetyl)-wortmannin to obtain a solution;
b. adding a tertiary amine or sodium bicarbonate to the solution;
c. adding mPEG-sulfhydryl 5000 to the solution of step (b);
d. stirring the solution of step (c) for 30 minutes;
e. adding ether to the stirred solution;
f. collecting the solid; and

g. washing the collected solid with ether to obtain the pegylated wortmannin derivative.

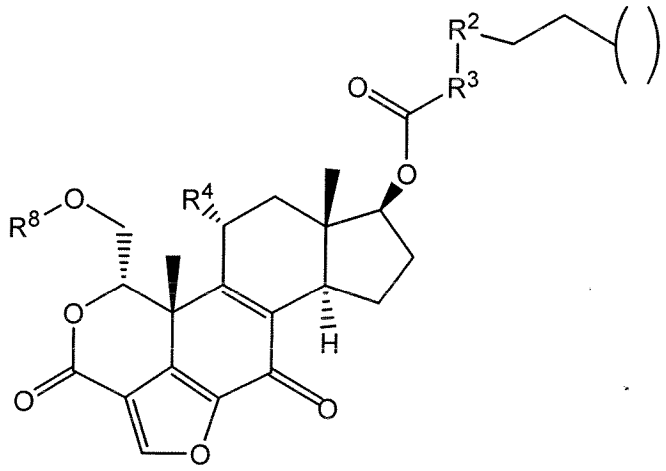
93. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula V:



V

wherein:

R^1 is alkyl, or a drug-polymer conjugate of a single non-repeating formula (V)



(B);

R^2 is -O-, -NH-, or -S-;

R^3 is alkyl, a cycloalkyl, or aryl;

R^4 is H, =O, -O-COC_4H_9, or OR^7;

R^7 is H, COR^9 or alkyl;

R^8 is alkyl or H;

R^9 is alkyl, H, aryl, or $-CH_2Ar$; and

n is 1-1000.

94. (Withdrawn) A process for the preparation of the compound of claim 93 comprising addition of an amine to a compound of claim 50 to obtain a compound of claim 93.

95. (Withdrawn) A process of claim 94 wherein the amine comprises diethyl amine.

96. (Withdrawn) A process for the preparation of a water-soluble drug-polymer conjugate of claim 74 comprising:

a) adding a solvent to 11-desacetyl-11-(1-iodoacetyl)-wortmannin to obtain a solution;
b) adding a tertiary amine to the solution;
c) adding mPEG-sulfhydryl 5000 to the solution of step (b);
d) stirring the solution of step (c) for 30 minutes;
e) adding ether to the stirred solution;
f) collecting the solid; and
g) washing the collected solid with ether to obtain the pegylated wortmannin derivative, as disclosed.